

A Balance-Chemograph

And the Excretion of Carbon Dioxide During Rest
and Work.

A Dissertation Submitted to the Faculty of the De-
partment of Literature, Science and the Arts
of the

UNIVERSITY OF MICHIGAN

In Partial Fulfillment of the Requirements for the
Degree of

DOCTOR OF PHILOSOPHY

by

GEORGE OSWIN HIGLEY, M. S. '93

Instructor in Chemistry, University of Michigan

ANN ARBOR, MICHIGAN,

MAY, 1905

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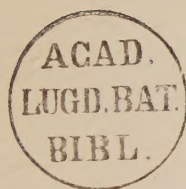
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Preface

This work was done in the physiological laboratory of the University of Michigan. The writer desires to express his thanks to Professor Warren P. Lombard for his continued and active interest in this research; to Professors S. L. Bigelow and Victor C. Vaughan for valuable suggestions; to Mr. W. P. Bowen in conjunction with whom the work of Sections III., VI., and a portion of VII. was done; and finally to friends who have so kindly served as subjects.

The work outlined in these papers was carried out with the Higley and Bowen respiration apparatus described in an article published in the American Journal of Physiology, Volume XII, 4, page 311. (1904.)

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A NEW CHEMOGRAPH AND SOME OF ITS PHYSIOLOGICAL APPLICATIONS

1. Introduction.

The graphic method dates from the invention of the Kymograph by Carl Ludwig in 1847. The superiority of this method over any method which involves the observing and recording of a series of phenomena by a single observer is obvious. "The graphic record includes more than can be grasped by any observer no matter how well trained. The records being preserved and read repeatedly, the chance of error is greatly reduced. Time relations can be worked out on a graphic record with a precision which can not be approached by direct observation." Applied first in the study of the character of complex cardiac and respiratory movements this method soon found numerous applications in the hands of the physiologist, the physicist and the engineer. It was not until recently, however, that the chemist seriously turned his attention toward a similar application of this method to a study of the course of chemical reactions.

In 1899 Ostwald¹, while engaged in an investigation of the remarkable behavior of chromium towards acids, was led by the great expenditure of time required to note at frequent intervals the indications of a gasburette, to devise an apparatus which should record automatically the rate of evolution of hydrogen. The gas was caused to flow from the generator through a long capillary tube, a pressure thus being produced approximately proportional to the rate of evolution of the gas. This pressure was caused to actuate a light lever by means of an ordinary tambour, and the curve of rate of solution of the metal was thus recorded upon a strip of paper. With this apparatus (the original chemograph) Ostwald demonstrated the periodic character of the chemical action; the effect upon the reaction of changes of temperature, and of concentration of acid; the effect of numerous reagents on the periodicity of the action; and the synchronism of changes in the rate of chemical action with those of the electrical tension of the metal. A consideration of Ostwald's paper leads to the conviction that the graphic method alone could have yielded such satisfactory results in the study of a problem of this kind.

So far as the writer was aware when this research was begun, no successful attempt had ever been made to determine the rate of a chemical change by recording the movements of a balance beam. However, in March, 1904, Professor G. N. Stewart, of Chicago University, while examining the apparatus to be described in this paper, stated that he had some time previously demonstrated the change in weight of a dialyzer filled with cane-sugar solution and suspended from the arm of a balance in a solution of pure water. By means of a lever attached to

the arm of the balance, a curve of change of weight of the dialyzer was recorded upon a drum. Professor Stewart's paper was read at a meeting of the Chemical Society of Owens College, Manchester, England, but was published only by title.

The idea of securing a continuous record of the carbon dioxide exhaled from the lungs by recording the movement of a balance, was suggested by Prof. W. P. Lombard as a possible means of explaining the changes in the pulse rate resulting from muscular work. Bowen² had found that in all vigorous work there are two well marked stages of increase in pulse rate, which are often separated by a period of uniform rate. First, there is an immediate and rapid rise, the primary rise, and later a more gradual secondary rise. The primary rise occurs so promptly after the beginning of work (latent period .8 of a second), that it could not be caused by the direct action of waste products on the heart centers. The secondary rise, however, which begins, with the most vigorous work done in the research (852 Kilogram metres per minute) one minute and twenty seconds after the beginning of work, might have been caused by the direct influence upon the heart of some waste product. The discovery of Loewy³ that tartaric acid, introduced into the jugular vein of an animal, markedly increases the respiratory volume, seemed to indicate that acid waste products thrown into the blood during the work might also be the cause of the secondary rise in pulse rate noted by Bowen. One of these acid waste products, carbon dioxide, was looked upon as a possible cause of the phenomenon mentioned. It was, therefore, believed that a graphic record of the changes in rate of excretion of this substance, placed by the side of the curve of the pulse rate might throw light on the cause of the change of the latter and could not fail to be of interest.

II. THE BALANCE-CHEMOGRAPH

1. Construction.

The apparatus for absorbing carbon dioxide and recording upon a blackened paper its rate of flow, is constructed as follows: (Fig. 1, Elevation). It consists of a Ruprecht lecture-room balance, capable of carrying a load of 6 kilograms in each pan and of turning to 5 milligrams. To the beam there was attached a copper tube one and one-half centimeters in diameter as shown by figure 2. Dry air containing carbon dioxide, enters at A through a short piece of very thin rubber tubing made of a surgeon's finger cot, passes through the portion designated by the arrows to the end of the beam and downward through two rubber connections like that just mentioned, and a glass tube D (Fig. 1) to the chamber for the absorption of carbon dioxide.

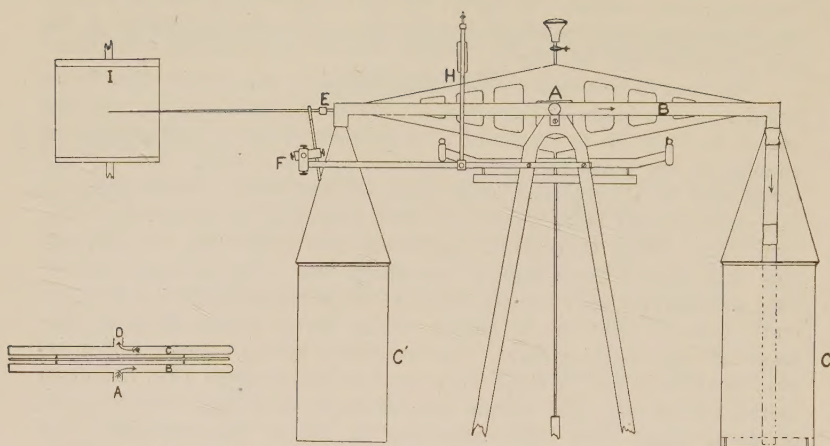


FIGURE 1.—This figure represents an elevation of the chemograph. The air enters at A and takes the direction shown by the arrows. C is the absorbing apparatus, and C' the counterpoise. Four gram-weights are placed upon the left beaker, and the lever-points thereby deflected upwards on the drum (I). The curve of carbon dioxide absorbed in C, is written downward to the right upon the drum.

FIGURE 2.—A horizontal section through the beam and balance tubes. The air passes through those portions only which are designated by arrows.

suspended upon the arm of the balance. (C Fig 1.) From the absorption apparatus the air passes upward through similar connections to the balance-tube C, back on the opposite side of the balance-beam to the center, where it leaves the balance through another piece of rubber tubing, and then passes into guard tubes G' and G'', which will be described later.

Absorption apparatus. (C, Fig 1). Several forms of absorption apparatus have been used in connection with the chemograph. That constructed for use in work experiments has been most employed and will be described here.

Since there was a question of removing the carbon dioxide from air flowing at the rate of 30 litres per minute during work, the absorption apparatus is necessarily large. It consists of a beaker 20 centimetres in diameter at the top, and 50 centimetres deep, with cover of thin copper, provided with openings two centimetres in diameter, into which are fitted the inlet and outlet tubes. The air passes downward into the beaker through a thin glass tube 2 centimetres in diameter,

to within about 2 centimeters of the bottom of the beaker, ending in an open space 3 centimeters deep and of a diameter equal to that of the beaker. (This open space was left because it was thought that the carbonic acid gas would thereby be more uniformly distributed throughout the whole cross-section of absorbent placed above.) The air now rises through about 5 kilograms of coarse, carefully screened soda-lime, and then through glass-wool covered with phosphorus pentoxide to hold back dust and the last trace of water formed in the reaction. This beaker when charged weighs about $5\frac{1}{2}$ kilograms. It is counterpoised by another beaker of the same exterior volume filled with spent soda-lime.

Recording Apparatus. In order to record the movements of the balance, there is attached to the end of the balance-beam a steel loop which engages the short arm of the light lever (E, Fig 1), made of two straws placed side by side and tipped, at the short end, with a steel wire, and at the long end with a piece of parchment paper. By means of an arrangement (F, Fig. 1) which will be clear from the figure, the fulcrum of the lever may be adjusted vertically, transversely, and horizontally. On the short arm of the recording lever (40 millimetres in length) there is placed a movable weight, by an adjustment of which the long arm (350 millimetres in length) is made to slightly preponderate. The lever records upon the drum the movements of the balance-beam magnified nine times. Since much depends upon the accurate adjustment of the writing lever upon the paper, the kymograph is set upon a base provided with ball-bearings and with two springs working against a screw, so that the kymograph may be rotated around a vertical axis and thus the drum be quickly and accurately adjusted to the recording lever at any time. Attached to the frame of the kymograph is a vertical brass rod to which are clamped three slender brass springs which extend horizontally and whose points may be brought into light contact with the paper on the drum. The middle one marks the level of the center of the fulcrum of the recording lever. This marker when once adjusted is, of course, never disturbed. The upper and lower ones draw lines marking the upper and lower limits of the excursion of the lever-point during calibration. They are readjusted from time to time as may be necessary.

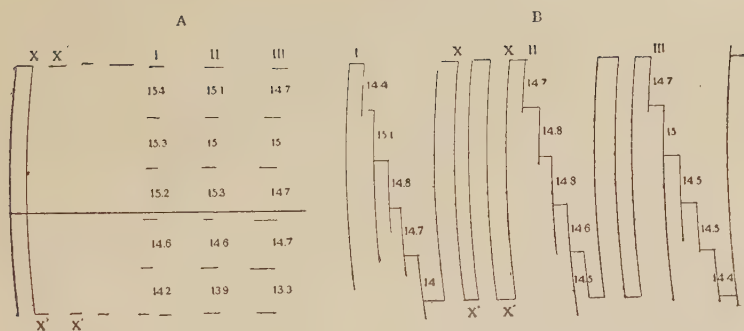
It has been already stated that the rubber connections of the balance were made very light in order to avoid, as far as possible, interference with the free movements of the balance. In order now to be able to write a curve of considerable length, representing, for example, a mass of five grams, it became necessary to diminish by some means the sensibility of the balance while interfering, as little as possible, with the uniformity of its movement. There was, therefore, attached to the frame of the balance, about ten centimetres from the central knife-edge, a steel yoke (H, Fig. 1) passing over the beam. From this yoke there was suspended a coil, five centimetres in length and about

one centimeter in diameter, made of phosphor-bronze wire .83 millimetres in diameter. This coil was attached at its lower end to the upper side of the beam of the balance by means of a hook, which together with the yoke could be set at any desired distance from the central knife-edge. A set screw, with a check-nut by which the upper end of the coil is attached to the yoke, admits of an adjustment of the tension of the spring at the will of the operator.

Adjustment of tension.—The balance is brought into equilibrium with spring disconnected. The spring is now attached to the beam and brought into a state of tension by turning the screw at the upper end of the coil, after which weights are placed upon the pan on the same side until equilibrium is again restored. In most of the work done with this apparatus the spring has had an initial tension of four grams.

We have here a combination of the beam and the spring balance. This apparatus was subjected to a series of careful tests in order to ascertain whether the records inscribed by it upon the blackened paper were of any value.

Tests of the balance: 1. Calibration. A careful test was made of the amount of vertical deflection of the end of the recording lever on the blackened drum produced by a mass of five grams. This was done as follows: The balance was brought into equilibrium. The beam was now arrested and five gram-weights were placed upon the counterpoise beaker; this produced an angular deflection of the beam of about 1 degree 45 minutes, and a vertical deflection of the recording lever-point of about 73 millimetres. After a delay of about 30 seconds to allow the lever to assume its position of rest, the screw controlling the position of the drum was carefully turned until the blackened paper was brought into light contact with the writing lever, and the kymograph was started and allowed to run until a short horizontal line had been drawn by the point of the recording lever upon the paper. The beam was now arrested, the weights removed, the beam again released, and the writing lever again allowed to come into a position of equilibrium. The kymograph was now started as before and a second light horizontal line drawn upon the paper. The vertical deflection of the writing point is a measure of the mass of five grams. This process was repeated many times, the weight being alternately added and removed to find out the accuracy with which the point of the writing lever returned to the same level as the drum. It was found that at the beginning of work, after the apparatus had stood for some hours, there was some irregularity at the first two or three movements of the beam. However, after a few minutes the movements became quite uniform. Starting, now, from the highest position of the recording lever, the gram weights were removed, one by one, the position of rest of the point of the lever being marked at each step by a short horizontal line as in the preceding case.



FIGURES 3A and 3B show the results of calibration of the chemograph with 5 gram-weights. The distances XX' are the vertical deflections of the recording-lever point for a mass of 5 grams added to the pan. The numbers represent the vertical deflection, in millimetres, of the lever point for ONE gram. A calibration of at least one series is made at the beginning of each experiment and often at the close also.

TABLE I (A).

	Series I.	Series II.	Series III.	Average.
Upper gram	15.4	15.1	14.7	15.06
Second gram	15.3	15.0	15.0	15.1
Third gram	15.2	15.3	14.7	15.1
Fourth gram	14.6	14.6	14.7	14.63
Fifth gram	(14.2)	(13.9)	(13.3)	
Total deflection	60.5	60.0	59.1	

TABLE I (B).

	Series I.	Series II.	Series III.	Average.
Upper gram	14.4	14.7	14.7	14.6
Second gram	15.1	14.8	15.0	15.03
Third gram	14.8	14.8	14.5	14.7
Fourth gram	14.7	14.6	14.5	14.6
Fifth gram	(14.0)	(14.5)	(14.4)	
Total deflection	59.0	58.9	58.7	

Fig. 3 A and Table I A show the results of one of these calibrations

in which are given the deflections due to one gram. Omitting the lower or fifth gram of each in A, we have the following averages. 15.06—15.1—15.1—14.6. The total deflection for four grams is, in the three series, 60.5, 60, and 59.1 millimetres, respectively. The extreme variation in deflection for the four grams is 1.4 millimetres or 2.3 per cent. and the greatest variation from the average of 0.7 millimetres, or 1.15 per cent. The greatest variation in deflection for a single gram (omitting the lower or fifth gram in each series) is 0.8 millimetres or 5.2 per cent.; the greatest variation from the average is 0.36 millimetres or 2.4 per cent. Figure 3 (B) and Table I (B) show the results of a calibration of the same apparatus, with slightly different tension in the spring. In this case the greatest variation in deflections for 4 grams and 1 gram are 0.3 millimetres or 0.5 per cent, and 0.6 millimetres or 4 per cent., respectively, and the greatest variation from the average, 0.2 millimetres or 3.2 per cent., and .38 millimetres or 2.5 per cent. The results of numerous calibrations showing that the deflection for the lower or fifth gram invariably gives low values, the use of this portion of the arc has been discontinued.

2. Test with a weighed quantity of mercury.—A small crystallizing dish, previously weighed upon a fine balance, was placed upon the right beaker, and the balance brought into equilibrium. Four gram weights were now added to the left beaker and the point of the lever thereby deflected vertically upward about 58 millimetres upon the drum. The usual calibration with 4 grams having now been made, the drum was started and a slow stream of mercury was allowed to flow into the crystallizing dish from a simple apparatus with capillary delivery tube. There was thus described upon the drum a short horizontal line, followed by a more or less regular curve inclining downward toward the right. Finally when about two grams of mercury had been allowed to flow in this manner into the crystallizing dish, the addition of mercury was discontinued, and the curve caused to end in a horizontal line. The beam was now arrested and the crystallizing dish removed. The vertical deflections of the writing lever due to the successive addition and removal of four grams in the initial calibration process were now determined. The average of these values is, of course, the graphical equivalent of four grams. From this there was readily obtained the modulus of the balance, viz.: the number of milligrams represented by one millimetre of vertical distance upon the drum. The vertical distance between the initial and final positions of the writing lever in the experiment with mercury was now measured, and the weight of mercury added obtained by multiplying the modulus by this value. Finally the crystallizing dish with its contents was reweighed upon a fine balance, and the weight of mercury thus determined compared with that obtained by the graphical method.

TABLE II.

Showing the results of calibration of Balance with Mercury.

Vertical deflecti'n for one gram	* Modulus M	Initial height of writing point = h.	Final height of writing point = h'	Weight graphi- cally deter- mined (h-h')M	Weight on fine balance	Error	Per cent. Error
Millime- tres		Millime- tres	Milli- metres				
11.63	0.0859	82.5	55.9	2.287	2.273	+0.014	+0.61
11.63	0.0859	55.9	26.4	2.537	2.5695	-0.0326	-1.26
11.63	0.0859	83.0	58.5	2.148	2.1624	-0.0144	-0.66
11.63	0.0859	58.5	34.6	2.055	2.0707	-0.0152	-0.70
14.57	0.0686	88.0	66.9	1.447	1.4331	+0.014	+0.98
14.57	0.0686	66.9	34.5	2.2237	2.2172	+0.0065	+0.29
14.57	0.0686	87.8	59.9	1.9149	1.9092	+0.0057	+0.3
14.57	0.0686	59.9	24.3	2.4434	2.4424	+0.001	+0.04
14.58	0.0686	88.0	76.0	0.823	0.847	-0.024	-2.8
14.59	0.0686	76.0	62.3	0.9396	0.9282	+0.0114	+1.23
14.59	0.0686	73.3	59.3	0.953	0.9488	+0.0031	+0.40
14.59	0.0686	59.3	42.7	1.139	1.177	-0.0213	-1.9

*Experiments 1-4 were made by the use of a brass spring; the following experiments with a phosphor-bronz spring of quite a different tension. This accounts for the widely different values of the modulus.

The results of a series of such tests are shown in Table II, in which there are given: Vertical deflection in millimetres of the lever-point for one gram added to the pan: Modulus (M) or the weight in grams corresponding to one millimetre deflection; initial height of writing lever-point "h"; Final height of lever-point h'; weight of mercury as graphically determined, (h-h') M; Weight of mercury as determined on fine balance. Error + or -, and per cent of error. It will be observed that the error was generally positive, and varied in the different experiments between .001 and .0326 grams, the average error being about .014 grams, or approximately .7 per cent.

3. Test with uniform current of Carbon Dioxide.—It will thus be seen that the working of the chemograph is more uniform and accurate when the weight is added gradually as in the case of the mercury and without arresting the motion, that when the weights are added a gram at a time with the necessary arrest of the beam. It was now thought desirable to test the character of the curve written by the lever as the result of a practically constant addition of weight to the absorption apparatus. Accordingly a current of carbon dioxide, as uniform as possible, was caused to flow for seven minutes through the apparatus, the drum meanwhile revolving uniformly. The result was a smooth

curve about 30 centimetres in length, which was a very close approximation to a straight line, measurements showing that at no point was the deviation from a straight line greater than .7 millimeters. This experiment was repeatedly performed with practically the same result.

It is evident that when the recording lever has reached the lower limit of the arc, the beam may be arrested, and additional weights added without interrupting the experiment and with a loss of only a small portion of the curve. This may be repeated for hours, enabling the operator to determine both the course of the reaction throughout its whole extent and the total weight of gas absorbed.

The method of determining the rate of the reaction during any period is as follows: With a radius equal to the length of the long arm of the recording lever, and with the proper points on the central reference line as centres, arcs are drawn cutting the time line at the beginning and the end of the desired period, and also the curve of carbon dioxide. The vertical distance between the two intersections of the carbon-dioxide curve by these arcs is the measure of the amount of that gas absorbed during the time cut off below. The modulus of the apparatus having been determined as described earlier, the rate of absorption between the desired limits is readily determined.

4. Test with a weighed quantity of carbon dioxide.—A series of experiments were now carried out with carbonic acid gas. There was set up a carbon dioxide apparatus consisting of a small fractionating flask provided with a dropping funnel and delivery tube, to which was attached a drying tube filled with pumice stone and sulphuric acid. Into this flask there was brought a quantity of a saturated solution of sodium carbonate, while sulphuric acid was placed in the dropping funnel. The apparatus was now carefully weighed, after which it was attached to the drying tube of the chemograph, a current of pure air free from carbon dioxide was drawn through it at the rate of half a litre per minute, and the sulphuric acid was slowly dropped upon the carbonate. The gas thus produced, diluted with seven litres per minute of purified outer air was drawn through the absorption apparatus of the chemograph, the kymograph drum meanwhile revolving at a uniform rate. This experiment was repeatedly tried, with the following results.

No.	Weight Carbon Dioxide.			
	By Loss in Weight.	Graphically.	Error.	Per Cent Error.
1.	2.4	2.33	.07	2.9
2.	3.548	3.487	.061	1.7
3.	1.810	1.815	.004	0.03
4.	2.933	2.83	.103	3.5
5.	3.152	3.192	.040	1.2

3. Uses.

It is evident that this form of chemograph may be used in a study of the course of many chemical reactions in which gas or vapor is evolved, since the apparatus will evidently write a curve of loss in weight as readily as of gain in weight. It is only necessary to place the generator upon the pan of the balance, to make the usual adjustments, and allow the process to continue as long as desired. A tracing of the course of a reaction in which there is an escape of hydrogen will, perhaps not be practicable with this apparatus, on account of the lightness of that gas. However, the curves of rate of loss of water, ammonia, carbon dioxide, etc., may be readily written.

III. METHODS OF DETERMINING THE RATE OF EXCRETION OF CARBON DIOXIDE FROM THE LUNGS.

1. Methods Previously Employed.

A great variety of methods have been employed by different investigators to determine the rate of excretion of carbon dioxide from the lungs. The methods are of two types: Respiratory Chamber Methods and Mask or Mouth Piece Methods.

a. Respiratory Chamber Methods.

The earliest form of respiratory chamber was a simple bell jar in which a small animal was confined, in some cases until asphyxiation resulted. Samples of the inclosed air were taken, as desired during the course of the experiment and at its close, and analyzed for carbon dioxide and oxygen. Such a method was made use of by Black⁴, Priestly⁵ Lavoisier and Laplace⁶, and others. It has recently been successfully employed by Haldane and Smith⁷ in a study of the question of existence of odorous substances in the air exhaled by a human subject. This method is, of course, open to the objection that there is a constant diminution in the amount of oxygen present in the chamber, and a corresponding increase in respiration products with disturbance of the normal respiratory exchange. In order to remove the objectionable features of this primitive apparatus, Lavoisier suggested two improvements which resulted in the development of two distinct forms of respiratory chamber which are in use at the present time. In the first form, that of Regnault and Reiset, the air of the chamber is circulated by means of pumps through a system of purifying tubes charged with concentrated sulphuric acid and with potassium hydroxide for the removal of water and carbon dioxide respectively; the oxygen is brought up to the normal amount by addition of a fresh supply from a gasometer and the air returned to the chamber. This apparatus has been employed in a modified form by Hoppe-Seyler and Stroganow¹ Pfluger and Colesanti⁸, and Atwater and Benedict⁹.

Lavoisier's second modification was developed by Scharling¹⁰. An animal was placed in a chamber consisting of a large cask, provid-

ed with inlet and outlet tubes. Air freed from carbon dioxide was drawn through the chamber, the moisture and carbon dioxide in the out-going air being absorbed by concentrated sulphuric acid and potassium hydroxide respectively. Samples of the air in the cask at the beginning and the end of the experiment were also taken and analyzed.

Since it was found difficult to maintain a sufficient ventilation and at the same time to secure complete absorption of carbon dioxide and water, Pettenkofer¹¹ modified this apparatus in the following manner: The total volume of air drawn through the chamber was determined by means of a meter. Continuous samples of the air entering and leaving the chamber were also taken, measured, and analyzed for carbon dioxide and water; the difference in the content of carbon dioxide and water in the two samples multiplied by the ratio of the total ventilation to the volume of the samples, gave the amount of carbon dioxide and water exhaled by the subject.

Pettenkofer's apparatus was further improved by Tigerstedt¹², was given a capacity of 100 cubic metres, and has since been extensively employed by Johannsen¹³, Atwater and others. This apparatus has many points of excellence some of which are as follows:

(1) It admits of experiments of indefinite length.

(2) It admits of making experiments upon eighteen or more persons at once, thus enabling the experimenter to obtain average values.

(3) In its most complete form as employed by Atwater¹⁴, it performs the work both of a respiration apparatus proper and of a calorimeter, giving results which are comparable in accuracy to those obtained by the use of the combustion calorimeter and the combustion furnace.

Quite recently there has appeared a respiratory chamber method by Jacquet¹⁵. In respect to capacity of chamber there is here a departure from modern methods, as it holds only two or three cubic meters. However, the samples of air, taken at intervals of one hour, are collected over mercury, and analyzed by the very accurate Petterson and Hogland method thus permitting a determination of oxygen as well as carbon dioxide.

(b) Mask and Mouthpiece Methods:

The first *quantitative* study of the respiration was made with the Mask method by Lavoisier¹⁶. This investigator in 1790, read, before the French academy, a paper in which a new method was described. The subject wore a mask (*tete du cuivre*) connected with a gasometer containing air. This air after passing into the lungs of the subject was exhaled through a huge tube filled with caustic potash solution, the increase in weight of which represented the carbon dioxide.

Method of Speck¹⁷. According to this method the subject, with closed nostrils, breathes through a mouth-piece from a spirometer, the air being collected in a second spirometer. At the close of the experiment a sample of air is drawn from the expiration spirometer and

its percentage of carbon dioxide and of oxygen determined by absorption with barium hydroxide and pyrogallol respectively.

Method of Geppert and Zuntz¹⁸. According to this method the expired air is forced through a carefully calibrated gas meter and its volume accurately measured. Samples of the air are taken by means of a special sampling device which is operated by the gas-meter itself. A number of tubes each with a capillary at the upper end, are filled to the tips with acid water. These are connected to a lowering device which is driven by a belt running over a pulley on the main axis of the gas-meter. As the air passes through the gas-meter the pulley revolves, the leveling tube connected with the collecting apparatus is gradually lowered and the collecting tube is thus filled with air, whose composition has been found to represent quite accurately that of the air passing through the meter. These samples of air are then analyzed for carbon dioxide and oxygen, and there is thus obtained both the carbon dioxide excreted and the oxygen absorbed, giving, of course, the respiratory quotient.

Method of Hanriot and Richet¹⁹. The method of these investigators is beautiful in principle. The outside air is drawn through an accurately calibrated gas-meter, is then inspired by the subject and expired through a second gas-meter. It now passes through an absorption apparatus charged with concentrated potassium hydroxide solution which dissolves the carbon dioxide, after which it is measured by a third gas-meter. If v represents the volume of inspired air, v^1 that of the expired air, and v^{11} that of the expired air deprived of carbon dioxide, it is evident that v^1 minus v^{11} represents the volume of carbon dioxide excreted, and v minus v^{11} represents the volume of oxygen absorbed.

2. Method Employed in This Research.

Each of the methods outlined above has its excellent features and has contributed to our knowledge of the respiration process; however, as a careful study showed no one of them to be adapted to a determination of the rate of change of carbon dioxide excretion, within short intervals of time, such as was demanded in this research, Mr. W. P. Bowen and the writer²⁰ devised the apparatus now to be described.

The subject breathes through a mask with valve-chamber for the separation of the inspired and expired air. The latter is dried by means of sulphuric acid, and is then freed from carbon dioxide by passing through the chemograph as described in a preceding section. The air now passes in succession through two guard-tubes and a gasometer and to a suction pump. The apparatus, which with the exception of mask, chemograph and pump, is shown in figure 4, is constructed in the following manner:

Mask. The subject respires through a mask made as follows: A

copper wire 2 millimetres in diameter is so bent as to fit over the bridge of the nose and the face, inclosing nose and mouth. A piece of heavy tin is then bent in the same form, that of an ovoid about 11 centimetres in length and 8 centimetres broad at the widest part. This is soldered to the wire, making the sides of a box about 4 centimetres in depth and rather closely fitting the face. The space between this edge and the face, is made air-tight in the following manner: A rubber tube, such as is used on the Townshend ether inhaler, is stretched on over the wired edge and fastened with cement. By inflating the tube and closing it off by means of a clamp, a cushion filled with air is brought between the face and the wired edge of the mouth piece. A sheet of rubber is stretched over the front of the box, and firmly cemented and wired in place. This is then pierced in the center and through it passes a short glass tube 1.2 centimeters in diameter, which is attached to the valve-chamber. Especial care was taken to make the volume of the tubes between the mouth and the valves as small as possible. The mask is held firmly to the face by wide elastic bands passing around the head.

Valve-chamber: (V, Fig. 4). The valve-chamber is of the same general form as that used by Zuntz and Schumburg²¹, except that it is made of glass instead of metal, thus permitting a view of the working of the valves. It consists of a large T tube, 20 centimetres in length and 4 centimetres in diameter, with a side tube 1.2 centimetres in diameter, to which the mouth piece is attached. The valve seats are

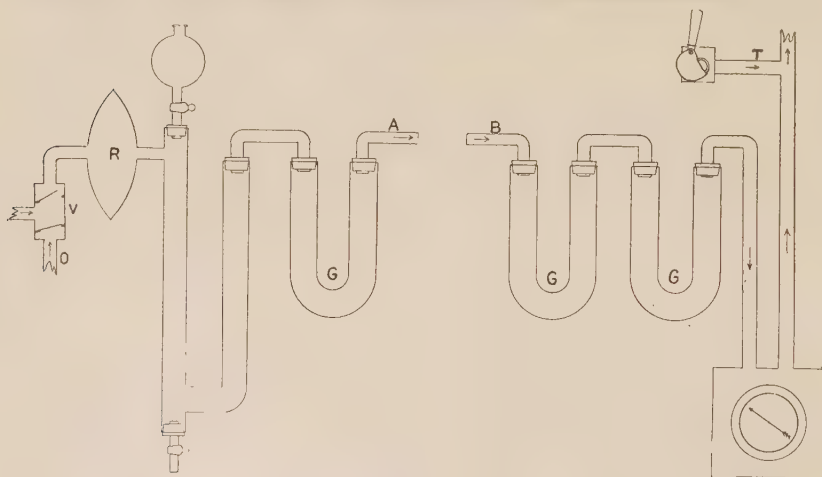


FIGURE 4.—The respiration apparatus except mask, chemograph and pump. Out-door air enters at O. R is the bag. The drying apparatus and guard tube are shown at G. A and B connect with the tubes of the chemograph. T is an auxiliary tube with adjustable valve, by means of which the flow of air through the main circuit may be regulated.

of cork covered with thin sheet-rubber fastened on with rubber cement. The openings are about 1.5 centimetres in diameter; the valves are made of thin sheet-rubber stiffened above with a disk of very thin aluminum foil attached by means of rubber cement. The out-door air enters the lower end of the valve-chamber through a wide glass tube. (O).

From the valve-chamber the air passes into a rubber balloon holding when moderately distended about 3 litres. At each expiration this balloon is somewhat inflated, but is deflated through the chemograph by the action of the pump during the next inspiration. There is thus a substantially uniform delivery of air to the chemograph.

It is often convenient to cause the expired air to pass for a time directly to the pump without passing through the chemograph. For this purpose a shunt is introduced in the main circuit beyond the balloon.

Drying Tubes. The apparatus for the removal of moisture consists, essentially, of a U tube 75 centimetres in length and 4 centimetres interior diameter, filled with coarse pumice stone saturated with concentrated sulphuric acid. This tube is followed by a guard tube (G Fig. 4), about 25 centimetres long, filled in the same manner. The completeness of the action of the preceding tube may be seen in the fact that the guard tube in no case gained more than .01 grams, and usually less than .005 grams, during an experiment in which air saturated with water vapor, and flowing at the rate of 30 litres per minute, passed through the train for 30 minutes.

From the guard tube the air flows through the absorption beaker of the chemograph, passing then through two guard tubes G' and G'' filled with pumice stone and sulphuric acid. The first of these tubes in an ordinary work experiment shows a gain of only .05 grams; the weight of the second remains practically unchanged. The air passes now, at the will of the operator, through a shunt tube containing clear lime-water as a test for the presence of carbon dioxide, then through an Elster gas-meter and to the pump.

Suction Pump. In order to relieve the lungs of the subject from the labor involved in forcing the expired air through the tubes and gas-meter, the latter is connected to the suction side of a number 2 American blower, capable of drawing air through the entire apparatus at the rate of 30 litres per minute. This amount of air is sufficient for a subject engaged in moderate muscular work, but its rate of flow is not equal to that at which air passes from the lungs during a vigorous act of expiration. The balloon previously mentioned is introduced in the circuit in order to permit the subject to exhale freely, the air expelled at one expiration being drawn from the balloon by the pump during the next inspiration.

It has already been stated that the suction pump is capable of drawing 30 litres of air per minute through the respiration apparatus. Since, however, in rest experiments the subject needs only 6 to 8 litres

of air per minute, some system of regulation was needed whereby the amount of air drawn through the apparatus could be adjusted at will. There was therefore introduced above the gasmeter a side tube (T Fig. 4) provided with an adjustable valve. When this valve is closed there is drawn through the train the amount of 30 litres per minute; when the valve is open the resistance of the short side tube is so slight that little or no air passes through the train. The handle of the valve passes over a graduated arc. A preliminary calibration process enables the operator to so set the valve that any desired volume of air up to 30 litres per minute will pass through the train.

Some of the advantages claimed for this respiration apparatus are the following:

(1) As a result of the excellent fit of the mask and of the relief afforded to the respiratory organs by the combination of balloon and suction pump, the conditions approach very closely to those of normal respiration. In fact, it has several times happened that a subject has fallen asleep during a rest experiment, after the mask had remained continuously upon the face for from one to three hours.

(2) This method permits of a determination of the carbon dioxide excreted during normal respiration within 2 per cent.

(3) This method obviates the necessity of taking samples of the expired air, and of making long and tedious analyses followed by complicated calculations. At the close of an experiment lasting an hour or more the total weight of carbon dioxide excreted by the subject may be ascertained in five minutes or less.

(4) By reason of the capacity of the chemograph to register changes in rate of absorption of carbon dioxide, the whole course of excretion can be determined.

IV. THE RELATION OF CARBON DIOXIDE EXCRETION TO BODY WEIGHT.

1. Introduction.

Considerable work has already been done in this field by Zuntz²² Johanssen²³, Magnus-Levy²⁴, Tigerstedt and Sonden²⁵ and others. The average results given in the form of carbon dioxide excretion per kilogram of body weight per minute are widely variable, as will appear by reference to Table III.

TABLE III.

Showing the Relation of Carbon Dioxide Excretion to Body Weight.

Conditions of Experiment.	Carbon Dioxide Excretion Grams per Kilogram and minute.	Observer.
1. Complete rest in bed; average for 24 hours	.0048	Johanssen.
2. Complete rest, sitting; average for 24 hours	.00516	Johanssen.
3. Complete muscular rest.....	.00512	Zuntz.
	.00484 }	
4. Ordinary rest in bed, average for 24 hours	.00578	Johanssen.
5. Complete muscular rest reclining from 9:35 a. m. to 7:21 a. m.....	.0058	Magnus-Levy.
6. Complete muscular rest, fasting.....	.00594	Magnus-Levy.
7. Nine persons sitting quietly, 10 a. m. until 3 p. m.....	.00792	Tigerstedt and Sonden.
8. Five persons doing no muscular work; average fasting value	.00756	Tigerstedt and Sonden.
9. Nineteen persons muscular rest, reclin- ing, 3:20 to 5:30 p. m.....	.0063	Higley.

These variations arise partly because the subjects during the experiments were in different degrees of muscular rest, and partly because the experiments were made at various lengths of time after meals, thus involving the variable work of the digestive organs. The great difference between the carbon dioxide excretion during absolute rest and during merely relative rest has been well shown by Johanssen. These experiments in which Johanssen himself, was the subject, were in part carried out while the subject was in the state of ordinary rest in bed and in part while all muscular tension was avoided as far as possible. In the former experiments the average carbon dioxide excretion per kilogram of body weight per minute was .0059 grams; in the latter series the average was only .0054 grams, a difference of 8.6 per cent. The posture of the subject also has a great influence on the intensity of the gaseous exchange. Thus Johanssen found the carbon dioxide excretion while the subject was sitting, to be 1.5 grams per hour more than while he was reclining, a difference of 7%. Katzenstein has observed, in parallel work, a difference of from 12 to 22% for this difference of posture.

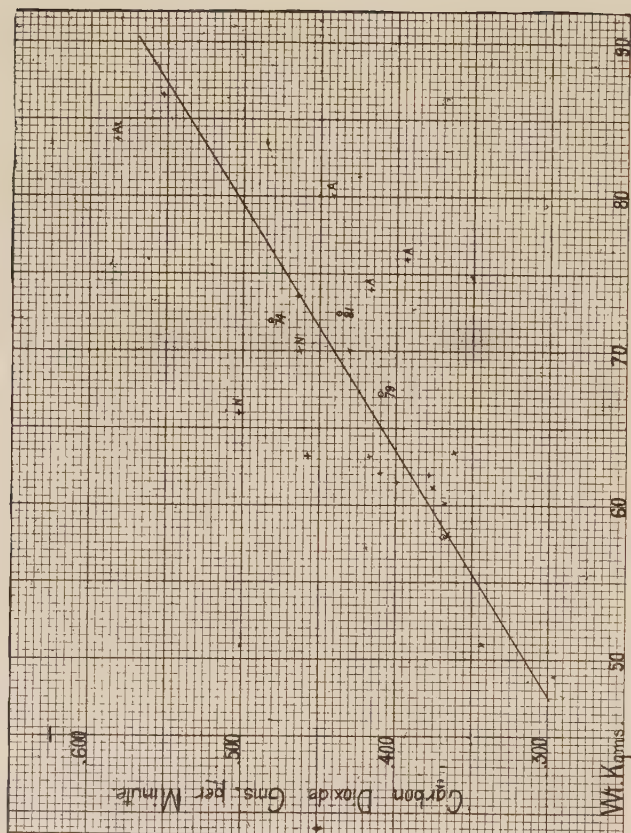


FIGURE 5—Relation of carbon dioxide excretion to body weight; curve of average excretion. At, athlete. A adipose tissue. 74 degree, 79 degrees and 81 degrees represent the average values for three subjects for the number of experiments indicated.

The experiments of Vierordt²⁶, Speck²⁷, and others have shown that the rate of excretion of carbon dioxide is increased 40 per cent as a result of the digestion process. This increase is attributed to the increase of work of the body due to the increased activity of the digestive organs, and also in part to conversion of carbohydrates into fats with separation of a large percentage of the oxygen of the former as carbon dioxide (Hanriot²⁸). From these results it follows that a uniform rate of excretion of carbon dioxide per kilogram of body weight in the case of a number of subjects or even with the same subject can not be expected, unless the experiments are carried out at approximately the same hour, and at about the same length of time after a meal which is approximately the same as to amount and character.

A number of persons, mainly medical students, having volunteered to act as subjects, the writer carried out experiments on the rate of excretion of carbon dioxide per kilogram of body weight.

It is not claimed that the experiments now to be described were carried out in an ideal manner, since the subjects were under the control of the experimenter only during the 20 minutes immediately preceding the experiment. Furthermore, in most cases the subjects had had no previous experience in similar work. However, the experiments were carried out at approximately the same time of day, the subjects partook of their midday meal at about the same hour, and the work of the subjects was about the same during the hours that intervened between the meal and the experiment. The subjects were engaged for the most part in Physiological laboratory work during the hours that intervened between the preceding meal and the experiment. All the subjects were apparently in good health except that two were troubled at the time with indigestion and two had colds.

(2) Method. The experiments were conducted as follows: Each subject in turn reclined upon a couch for about 15 minutes preceding the beginning of the work. The mask was now adjusted and, at the end of a further period of 5 minutes the experiment began. Great pains were taken that the subject should be in a state of as complete muscular rest as possible.

(3) Results. The results are shown in table IV in which are given: sex; age; weight of subject (exclusive of clothing) in pounds and kilograms; date; time elapsed since preceding meal; length of experiment; carbon dioxide excretion in grams per minute, and in grams per minute per kilogram of body weight; **remarks**.

TABLE IV.

Table Showing Relation of Body Weight to Carbon Dioxide Excretion:

No.	Sex	Age	Weight without Clothing		Date	Time Since Preceding	Length of Ex- perim't	Carbon Dioxide Excretion Per Min.	Per Min. & Kilo Body Weight Grams.	Remarks
			lbs	Kilos	Mo. Day Hr.	ing Meal	Minut's	Grams.		
1	M	23	135	61.5	3 7 3.50	3.5 hrs.	10	.400	.0065	Adipose tissue
2	M		167	76	3 7 4.20	4	10	.393	.0056	
3	M	20	137	62.2	3 9 4.40	4.25	10	.377	.006	
4	M	20			3 9 5.00	4.75	10	.348		
5	M	21	137	62.2	3 14 4.00	4	6	.410	.0065	Catarrh infec'n
6	M	20	126	57.3	3 14 4.20	4	7	.420	.0073	
7	M	20	139	62.2	3 14 5.20	5	7	.417	(.0066)	
8	F	30	107	49	3 16 4.15	4	8	.297	.006	
9	F	19	112	51	3 16 4.45	4.5	6	.341	.0067	Adipose tissue
10	F	30	176	540	3 16 5.30	5.20	6	.442	.0055	
11	M	20	33	60.2	3 18 4.00	3.75	4	.366	.0061	
12	M	21	115	52.3	3 18 4.15	4	3	.283	.0054	
13	M	22	145	66	3 18 4.30	4	5	.503	(.0076)	Nausea
14	M	21	162	73.6	3 19 3.20	3	6	.465	.0063	
15	M	27	190	86.4	3 19 3.20	3.5	5	.552	.0064	
16	M	22	129	58	3 19 4.00	3	5	.368	.0063	
17	M	25	158	71.6	3 19 4.00	3.5	5	.519	.0076	Slight nausea Athlete
18	M	21	135	561.2	3 21 3.50	3.5	5	.376	.0061	
19	M	26	154	570	3 21 4.00	3.5	7	.463	(.0066)	
20	M	26	184	82.9	3 21 4.35	4.25	5	.583	.0069	
21	M	21	139	63.1	3 21 5.00	4.5	4	.458	.0073	Adipose tissue
22	M	4	163	74.1	3 21 5.20	5	5	.418	.0056	
23	M	45	141	63.5	3 25	9	9	.361	.0057	Catarrhal in'fn
24	M	29	154	70	3 28 5.30	5	3	.431	(.0062)	
Average .0063										

In this average all bracketed numbers are omitted.

The results are also shown in a curve (Fig. 5), with body weight in kilograms as abscissae, and grams of carbon dioxide excreted per minute as ordinate. The curve was drawn as follows: The points representing the excretion of the various subjects were first plotted in the usual manner. The average excretion of carbon dioxide per minute per kilogram of body weight (.0063 grams) having been found, the total excretion per minute was calculated for a hypothetical person having a body weight of 50 kilograms. This formed one point on the curve of average excretion. The value for subject 14 which coincided with the average, formed a second point. These points were now connected by a straight line giving, of course, the curve of average excretion for a subject of any weight.

This average, it will be observed, is approximately the mean of the lowest result obtained by Johanssen .0048 grams (see table III) and the highest result by Tigerstedt and Sonden .00792 grams. It is about 5% higher than the average of the results of Johanssen and Magnus-Levy (experiments 4, 5, and 3, table III). This result was obtained on a class of persons who were for the greater part exceptionally vigorous. Furthermore, with few exceptions, the subjects were acting for the first time as subject in a respiration experiment. Had the experiment been repeated several times with each subject, the average results would perhaps have been somewhat lower than that given in table III.

3. Results: It will be noted that the rates of excretion of carbon di-

oxide of subject number 8, a woman having a body weight of 40 kilograms, and of number 15, a man weighing 86.4 kilograms, was nearly the same, the value for each closely approximating the average; also that the subjects whose values vary widely from the average, belonged, for the greater part, to one of these two classes. *a.* Those whose values are represented on the chart by Ad. The low results in these cases (2, 10, 22) was probably due to the large amount of adipose tissue present in the body, since the metabolism in this form of tissue is very weak. *b.* Those whose values are represented by N on the chart. Those indicated in this manner were troubled with indigestion, number 13 having had severe nausea, and number 20 slight nausea at the time of the experiment.

4. Conclusions.

1. In a series of experiments such as that described in this section, the results are modified somewhat, in individual cases, by the state of health of the subject. Colds and indigestion apparently increase the rate of excretion of carbon dioxide per unit of body weight.

2. The amount of carbon dioxide excreted per kilogram of body weight is apparently greatly lowered by adipose tissue present in large amounts in the body of the subject.

V. INFLUENCES WHICH MODIFY THE RATE OF EXCRETION OF CARBON DIOXIDE DURING REST.*

Introduction. This work was suggested by that of Lombard²⁹ on "Some of the influences which affect the power of muscular contraction." In that research, which was made with the ergograph, Lombard found that, in general, there was a fall of muscular power during the day, this result being noted on eighteen out of a series of twenty-three days. However, on certain days, the fall in power due to fatigue was slight and on five days the power was greater at the last experiment than at the first. These exceptions led to the suspicion that barometric changes had an influence on muscular endurance. When later a comparison was made between Lombard's endurance curve and the curve of barometric height, it was found that, while no constant relationship existed between the two variables, they varied in the same sense on twenty out of twenty-three days; *i. e.*, in general "when the barometer rose during the day, or fell less than on the preceding day, the muscular endurance either rose, or fell less than on the preceding day."

It has been shown furthermore, that while a diminution of barometric pressure increases both the respiration rate and the volume of air respired, after allowance is made for the increase of volume due to the lower pressure the volume respired is less (Speck).

Now, the effect of increasing barometric pressure upon the power of the muscular system might possibly be due to some influence

* This paper was accepted for publication by the officers of Section VIII, *d.* Eighth International Congress of Applied Chemistry, and was read before the Section at a stated meeting on September 11, 1912; BIOCHEMICAL BULLETIN, 1912, ii, p. 153.

exerted through the nervous and circulatory systems tending to increase the readiness of metabolism; if such were the case then a variation in barometric height should be accompanied by a variation, in the same sense, in the rate of excretion of carbon dioxide.

Plan of the experiments. It seemed that a series of experiments carried out for a month on three healthy subjects might throw light on this question, and also give interesting results as regards the effect of other conditions on the rate of carbon dioxide excretion. A series of respiration experiments was planned, accordingly, for three subjects, *A* and *B*, students in the University of Michigan, and the writer, *C*. *A* and *B* were 24 and 22 years of age respectively, and weighed, without clothing, 158 and 159½ pounds. *C* was 46 years of age and weighed, exclusive of clothing, 148 pounds. Each subject was to live his regular daily life except that no vigorous muscular exercise was to be engaged in immediately preceding any experiment, and that nothing whatever was to be eaten between meals. The plan of work is indicated in the appended summary, where the data for the third part of each experiment are placed below those for the first and second:

Subject	Hour of Rising	Reclined	First experiment	Breakfast	Time until next experiment	Reclined	Second experiment begun	Dinner
<i>A</i>	6	6:45	7:00	7:40-8:00	4 hr.	11:45	12:00	12:40
<i>B</i>	6	7:05	7:20	8:00-8:20	4 hr.	12:05	12:20	1:00
<i>C</i>	6	7:25	7:40	8:00-8:20	4½ hr.	12:25	12:40	1:00

Subject	Time until next experiment	Reclined	Third experiment begun	Lunch	Experimenter
<i>A</i>	4 hrs.	4:45	5:00	5:40	<i>C</i>
<i>B</i>	4 hrs.	5:00	5:20	6:00	<i>A</i>
<i>C</i>	4½ hrs.	5:25	5:40	6:00	<i>B</i>

The routine of work was as follows: The subjects rose at 6 o'clock reaching the laboratory at about 6:35. *A* reclined upon a couch at 6:45 in preparation for the first experiment. *B* and *C* prepared all the apparatus, making the initial calibration of the balance, weighing the guard tubes, reading and recording the barometric height, the outdoor and room temperature, etc. In order to enable the experimenter to judge the better as to the physical condition of each subject, mouth temperature and pulse were also taken and recorded. This routine at the laboratory was followed at 12 M. and 5 P. M.

TABLE IV.

Data showing the excretion of carbon dioxide by subjects *A*, *B*, and *C*, in milligrams per minute

Date	Subject <i>A</i>			Subject <i>B</i>			Subject <i>C</i>		
	7 A. M.	12 M.	5 P. M.	7 A. M.	12 M.	5 P. M.	7 A. M.	12 M.	5 P. M.
December									
23	406	422	—	381	498	567	406	390	447
24	438	460	447	489	422	541	419	409	409
26	442	448	466	514	429	(743)	422	403	428
27	422	453	466	535	434	548	390	403	390
28	403	448	(635)	488	507	498	397	375	419
29	407	422	381	520	553	546	382	387	456
30	438	483	405	529	495	518	419	381	374
31	425	470	444	(647)	489	476	390	362	438
Jan.									
2	433	487	480	438	(611)	570	393	422	473
3	470	436	422	416	462	508	394	377	422
4	507	435	480	537	442	553	—	386	448
5	469	473	442	528	466	515	410	—	396
6	458	466	442	—	525	531	449	403	476
7	465	442	432	439	560	466	406	386	411
9	416	436	436	410	442	462	390	380	448
10	416	459	448	455	506	—	383	425	473
11	456	439	426	453	422	526	363	402	337
12	446	—	—	543	—	—	388	—	—
13	—	—	—	—	—	—	—	—	—
14	405	462	445	—	476	504	398	427	—
16	436	496	449	469	531	440	402	396	437
17	412	453	—	418	460	—	—	459	—
18	377	407	462	—	459	469	364	442	435
19	472	487	422	445	474	409	403	438	429
20	469	476	436	402	455	432	402	474	419
21	462	436	493	399	442	493	406	448	434
23	428	481	429	509	442	436	396	449	429
24	422	517	495	500	459	537	409	460	429
25	422	475	402	—	528	486	422	468	428
26	495	561	—	—	—	—	422	422	—
Averages	438	462	443	472	476	501	401	414	427

Results. The result of this series of experiments are shown in Table IV in miligrams of carbon dioxide excretion per minute. It will be noted that A's average for the mid-day experiments is considerably higher than that for the morning and evening experiments. This is due in part, at last, to the fact that this subject took his heartiest meal in the morning. The excretion of carbon dioxide for B and C, on the other hand, was greatest in the evening, since these subjects took their dinner at 1 p. m.

The remarkably high excretion shown for A at the evening experiment of December 28 (635 mg., while the average for that hour for this subject is only 443 mg.) is explained as follows: This subject went skating in the afternoon of that day and at about 2:30 o'clock had the misfortune to break through the ice, becoming wet to the neck. On being rescued, he walked about two miles in his frozen clothing, exposed meanwhile to a strong wind at a temperature of about -6° C. On reaching his room he took a thorough rubdown, made a change of clothing, rested for one and one-half hours, and appeared at the laboratory at the usual hour for the experiments, with the result stated above. It will be noted that all of this subject's values for the following day, especially that of the evening, were much below the average, indicating a reaction from the exposure and excitement of the preceding day. The high excretion of the morning of January 4 is supposed to be due to lunch eaten late on the preceding evening; that of 12 o'clock, January 26, to an exceptionally heavy morning meal; and the low result of the evening of January 19 to an especially light midday meal.

The irregularity of results obtained from B are somewhat difficult to explain. Those of the morning of December 27, 30 and 31, were due to lunch eaten late the preceding evening and in the case of the two latter results, also in part to excessive haste to reach the laboratory in time for the regular experiment. Other high results, especially those of 5 p. m., December 26, and of 12 m., January 2, were undoubtedly due to indigestion.

Passing now to a study of the relation of carbon dioxide excretion to barometric changes, Figure 6 will be found to embody, in the form of curves, the results already given in Table IV, with time as abscissae, and miligrams of carbon dioxide per minute as ordinates; it presents curves for A, B and C, together with that for the barometer in millimeters of mercury and of the outdoor temperature in degrees centigrade. The temperature of the room was practically constant throughout the series of experiments. Three curves are given for each subject where the necessary data were at hand. *In each case the morning, midday and evening curves are represented, respectively, by solid, long-dash and short-dash lines.*

Analysis of the Results. *Comparison of the data for barometric pressure and carbon dioxide excretion.* Before proceeding to a rigorous mathematical investigation of the relationship between barometric change and carbon dioxide excretion, it seemed desirable to make a

comparison of these two variables at a number of the dates on which especially marked barometrical fluctuations took place, since in such cases the effect would be more pronounced and less likely to be masked by other varying conditions, such as amount and character of the preceding meal, character of muscular exercise, etc. To facilitate such a comparison, Tables V., VI., and VII, were prepared; they indicate experiment number; dates between which the comparison is made; barometric height, rise or fall; subject, carbon dioxide for the two days between which comparison is made; rise or fall of excretion; and relation between barometric change and carbon dioxide excretion, whether *direct* or *inverse*. Taking first the morning values, it was found that the barometer rose between 7 a. m., December 23, and 7 a. m., December 24, from 739 to 746, or 7mm. During the same period the excretion of carbon dioxide of the three subjects changed as follows: That of *A* from 406 to 438 mg. per minute, an increase of 32 mg.; that of *B* from 381 to 489, an increase of 108 mg. and that of *C* from 406 to 419, an increase of 13 mg. per minute. Thus with *rising* barometer there was an *increase* in the rate of excretion of carbon dioxide in the case of each subject. A similar result is obtained in four other morning experiments (two subjects). In three morning experiments there are two direct results each. One experiment shows two *indirect* results, *i. e.*, there is a change in carbon dioxide excretion which is opposite in sign to that in the barometer.

Summing up the results of the morning experiments we have the following: Eleven experiments were carried out on *A*, seven on *B*, and eleven on *C*. The degree of correspondence of barometric change with carbon dioxide excretion was:

- A, 7 cases out of 11, or 63.6 per cent.
- B, 6 cases out of 7, or 85.7 per cent.
- C, cases out of 11, or 55.5 per cent.

MGM CO₂
PER
MINUTE

500

A

450

400

350

300

250

200

B

500

450

400

350

300

250

200

C

450

400

350

300

250

200

760

740

720

BAR

° 10

0

-10

TEMP.

23

25

27

29

31

2

4

6

8

10

12

14

16

18

20

22

24

26

FIGURE 6—Curves showing CO₂ excretion by subjects A, B and C, in mg. per minute. *Morning*: solid lines; *midday*: long dash lines; *evening*: short-dash lines. (See Table I.) Note corresponding curves for barometric pressure and out-door temperature.

TABLE V—Data obtained at 7 a. m.

No	Date Dec.	Barometer			Subject	Excretion of carbon dioxide			Relation be- tween barome- tric change & carbon diox- ide excretion	
		Heights, mm	Rise, mm	Fall, mm		Per minute mg.	Rise, mg.	Fall, mg.	Direct	Inverse
1	23-24	739-746	7.	—	A	406-438	32	—	32	
					B	381-489	108	—	108	
					C	406-419	13	—	13	
2	26-28	745.1-721	—	24.1	A	442-403	—	39	39	
					B	514-488	—	26	26	
					C	422-397	—	25	25	
3	28-29	721-742.1	21.1	—	A	403-407	4	—	4	
					B	488-520	32	—	32	
					C	397-382	—	15	—	15
4	29-31	742.5-736	—	6.1	A	407-425	18	—	—	18
					B	—	—	—	—	
					C	382-390	8	—	—	8
5	Jan. 2-4	737.1-743.5	6.4	—	A	433-507	74	—	74	
					B	438-537	99	—	99	
					C	393-394	1	—	1	
6	5-7	743.5-732.5	—	11.	A	469-465	—	4	4	
					B	528-439	—	89	89	
					C	410-406	—	4	4	
7	11-12	753.9-737.1	—	16.8	A	456-446	—	10	10	
					B	453-543	90	—	—	90
					C	363-388	25	—	—	25
8	12-14	737.1-751.2	14.1	—	A	446-405	—	41	—	41
					B	—	—	—	—	
					C	388-398	10	—	10	
9	18-19	748.1-739.3	—	8.9	A	377-472	95	—	—	95
					B	—	—	—	—	
					C	364-403	39	—	—	39
10	23-24	749-739.8	—	9.2	A	428-422	—	6	6	
					B	509-500	—	9	9	
					C	396-409	13	—	—	13
11	24-26	739.8-758.8	19.	—	A	422-495	73	—	73	
					B	—	—	—	—	
					C	409-422	13	—	13	

The direct result from the midday experiments were as follows:

- A, 3 cases out of 7, or 42.8 per cent.
- B, 3 cases out of 9, or 33.3 per cent.
- C, 6 cases out of 9, or 66.6 per cent.

From the evening experiments the direct results were:

- A, 3 cases out of 6, or 50 per cent.
- B, 4 cases out of 9, or 44.4 per cent.
- C, 4 cases out of 8, or 50 per cent.

TABLE VI.

Data obtained at 12 m.

Dec.

No.	Date	Barometer	Rise	Fall	Subject	Carbon Dioxide	Rise	Fall	Direct In verse
1	23-24	739.1-746.2	7.1		A	422-460	38		38
					B	498-422		76	76
					C	390-409	19		19
2	26-28	742.5-726.9		15.6	A	446-448			
					B	429-507	78		78
					C	403-375		28	28
3	28-29	726.9-742.5	11.6		A	448-422		26	26
					B	507-553	46		46
					C	375-387	12		12
Jan									
4	29-31	742.5-736.1		6.4	A	422-470	48		48
					B	553-489		64	64
					C	387-362		25	25
5	2-4	738.9-745.1	6.2		A	487-435		52	52
					B	(611-442)		169	169
					C	422-386		36	36
6	5-7	743.5-732.9		10.6	A	473-442		31	31
					B	466-560	94		94
					C	403-386		17	17
7	18-19	747.7-740.1		7.8	A	407-487	80		80
					B	459-474	15		15
					C	442-438		4	4
8	23-24	749.8-738.8		11.	A	480-517	37		37
					B	442-459	17		17
					C	449-460	11		11
9	24-26	738.8-758.5	19.6		A	517-561	44		44
					B	459-528	69		69
					C	460-422		38	38

TABLE VII.

Data obtained at 5 p. m.									
No.	Date	Barometer	Rise	Fall	Subject	Carbon Dioxide	Rise	Fall	Direct In- verse
Dec.									
1	23-24	739.1-747.1	8		A	—			
					B	567-541		26	26
					C	447-409		38	38
2	26-27	741.5-718.2		12.9	A	466-466			
					B	(743-548)		195	195
					C	428-390		38	38
3	27-28	718.2-738.1	19.9		A	466-635	169		169
					B	548-498		50	50
					C	390-419	39		39
4	29-31	742.5-737.5		5	A	381-444	63		63
					B	546-476		70	70
	Jan.				C	456-438		18	18
5	2-4	740-745		5	A	480-480			
					B	570-553		17	17
					C	473-448		25	25
6	5-7	744.1-732.9		11.2	A	442-432		10	10
					B	515-466		49	49
					C	396-411			15
7	18-19	742.9-739.5		3.4	A	462-422		40	40
					B	469-409		60	60
					C	435-429		6	6
8	23-24	747.8-740		7.8	A	429-495	66		66
					B	436-537	101		101
					C	429-429			
9	24-25	740.755.1		15.1	A	495-402		93	93
					B	537-486		51	51
					C	429-428		1	1

Or, out of a total of seventy-seven experiments, there was direct relationship between barometric change and and carbon dioxide excretion in forty-two experiments, or 54.5 per cent.

It will be seen from these results that the apparent degree of correspondence, so far as it is revealed by this method of analysis, is greater in the morning experiments than in those carried out at midday or in the evening. This is probably due to the fact that in the morning not merely the digestive organs, but the whole system, is in a more uniform condition than at any other time during the twenty-four hours.

Application of the method of least squares. It now seemed desirable to subject the results obtained in this series of experiments to a more rigorous analysis than that just described, with a view of discovering what is the degree of correlation between the two variables, the

barometric height and the rate of excretion of carbon dioxide, during muscular rest. The data obtained in the experiments were, therefore, examined by the method of least squares, which was applied separately to the three sets of data from each subject in order that the effect of different times of day might be determined separately.

In Table VIII are given the barometric height and the corresponding carbon dioxide excretion†; the problem is to find the correlation between these two quantities, and also the regression of carbon dioxide on barometric height, *i. e.*, the amount of change in excretion of carbon dioxide for a millimeter change in barometric height. The means of columns 1 and 2 are obtained in the usual manner, by dividing the total in each column by the number of experiments (N). Having obtained these means, two additional columns are formed, giving the deviation of each observation from the mean of its column. In columns 5 and 6 are entered the squares of the deviations (X^2 and Y^2). The standard deviation (σ_1) is now obtained by dividing the sum of the squares in the fifth column by the number of experiments, N , and extracting the square root of the quotient; the standard deviation for y is, of course found in the same manner.

$$\sigma_1 = \sqrt{\frac{\sum x^2}{N}} = \sqrt{\frac{1769.71}{29}} = 7.8 \text{ and } \sigma_2 = \sqrt{\frac{\sum Y^2}{N}} = \sqrt{\frac{24951}{29}} = 29.3$$

* The data are those obtained from morning experiments on subject A.

Relation of Carbon Dioxide Excretion to Barometric Change.

TABLE VIII—7 A. M.

Barometer Millimetres	Carbon Dioxide Milligrams	x	y	x ²	y ²	Products (x y) Negative Positive
739	406	—4	—32	16	1024	128
746	438	3	0	9	—	—
745.1	442	2.1	4	4.41	16	8.4
726.2	422	—16.8	—16	282.24	256	268.8
721	403	—22	—35	484	1225	770
742.1	407	—0.9	—31	.81	961	27.9
740	438	—3	0	9		
736	425	—7	—13	49	169	91
737.1	433	—5.9	—5	34.81	25	29.5
741.3	470	—1.7	32	2.89	1024	54.4
743.5	507	.5	69	.25	4761	34.6
743.5	469	.5	31	.25	961	15.5
742.3	458	— .7	20	.49	400	14
732.5	465	—10.5	27	110.25	729	283.5
751.5	416	8.5	—22	72.25	484	187
751.4	416	8.4	—22	70.86	484	184.8
753.9	456	10.9	18	118.81	324	196.2
736.1	446	—5.9	8	34.81	64	47.2
751.2	405	8.2	—33	67.24	1089	270.6
746.5	436	3.5	—2	12.25	4	7
747.8	412	4.8	—26	23.04	676	124.8
748.2	377	5.2	—61	27.04	3721	317.2
739.3	472	—3.7	34	13.69	1156	125.8
745.5	469	—2.5	31	6.26	961	77.5
743.7	462	.7	23	.49	576	16.8
749.	428	6.	—10	36	100	60
739.8	422	—3.2	—16	10.24	256	51.2
747.9	422	4.9	—16	24.01	256	78.4
758.8	495	15.8	57	249.64	3249	900.6
				1769.71	24951	1754.7
						2622.7
						1754.7
						868.

$$\sigma_1 = \sqrt{\frac{1769.71}{29}} = 7.8$$

$$\sigma_2 = \sqrt{\frac{24951}{29}} = 29.3$$

$$\Sigma xy = 868$$

$$\text{Coefficient of correlation} = \frac{\Sigma xy}{N \sigma_1 \sigma_2} = \frac{868}{29 \times 7.8 \times 29.3} = .12$$

$$\text{Regression} = \frac{12 \sigma_2}{\sigma_1} = .45$$

The products XY are now collected, the negative in column 7 and the positive in column 8, and the totals determined. We have, then, $\Sigma(XY)=2622-1754.7=+868$.

From this coefficient of correlation (r) is obtained:

$$r = \frac{\Sigma(xy)}{N\sigma_x\sigma_y} = \frac{868}{29 \times 7.8 \times 29.3} = +.12$$

The positive sign of this coefficient indicates, of course, that the relationship between barometric change and carbon dioxide excretion in this case is *direct* or that the two variables change in the same sense. Since a coefficient of correlation of 1 indicates *perfect correlation*, the result obtained in the series of experiments represented in Table IV indicates a slight degree of correlation. The probable error of a correlation coefficient of this value for a series of 25 observations is at least 0.13 so that the value of r is 0.12 ± 0.13 .

Relation of carbon dioxide excretion to barometric change.

TABLE IX—A.—12 m.

Barometer reading, mm	Carbon dioxide excretion, mg.	X	Y	X ²	Y ²	Products (XY)	
						Negative	Positive
739.1	422	— 4.2	40	17.64	1,600	—	168
746.2	460	2.9	— 2	8.41	4	5.8	—
742.5	448	— 0.8	14	0.64	196	—	11.2
722.1	453	—21.2	— 9	449.44	81	—	190.8
726.9	448	—16.4	14	268.96	196	—	229.6
742.5	422	— 0.8	40	0.64	1,600	—	32
740.1	483	— 3.2	21	10.24	441	67.2	—
736.1	470	— 7.2	8	51.84	64	57.6	—
738.9	487	— 4.4	25	19.36	625	110.	—
742.9	436	— 0.4	26	0.16	676	—	10.4
745.1	435	1.8	—27	3.24	729	48.6	—
743.5	473	0.2	11	0.04	121	—	2.2
739.9	466	— 3.4	4	11.56	16	13.6	—
732.9	442	—10.4	20	108.16	400	—	208
745.8	436	2.5	26	6.25	676	65	—
753.2	459	9.9	— 3	98.01	9	29.7	—
749.3	439	6.6	23	36.00	529	151.8	—
753.6	462	10.3	0	106.09	0	—	—
747.5	496	4.2	34	17.64	1,156	—	142.8
748.1	453	4.8	— 9	23.04	81	43.2	—
747.9	407	4.6	55	21.16	3,025	253.0	—
740.1	487	— 3.2	25	10.24	625	80.	—
741.1	476	0.8	14	0.64	196	—	11.2
743.9	436	0.6	26	0.36	676	15.6	—
749.8	481	6.5	19	42.25	361	—	123.5
738.8	517	— 4.5	55	20.25	3,025	247.5	—
752.9	475	9.6	13	92.16	169	—	124.8
758.4	561	15.1	99	228.01	9,801	—	1,494.9
				1,642.43	27,078	1,174.6	2,749.4
							1,174.4

1,574.6

$$\sigma_1 = \sqrt{\frac{1,642.43}{28}} = 7.65, \quad \sigma_2 = \sqrt{\frac{27,078}{28}} = 31.1$$

$$\Sigma(xy) = 1,574.6$$

$$\text{Coefficient of correlation: } \frac{\Sigma(xy)}{N\sigma_1\sigma_2} = \frac{1,574.6}{28 \times 7.65 \times 31.1} = +0.236$$

$$\text{Regression} = \frac{0.236\delta_2}{\delta_1} = 0.95$$

Relation of Carbon Dioxide Excretion to Barometric Change.

TABLE X—A, 5 P. M.

Barometer Millimetres	Carbon Dioxide Milligrams	X	Y	X ²	Y ²	Products (xy)	
						Negative	Positive
741.1	447	4.1	4	16.81	16		16.4
741.1	466	—1.9	23	3.61	529	43.7	
718.2	466	—24.8	23	615.04	529	570.4	
742.5	381	— .5	—62	.25	3844		31
739	405	—4	—38	16	1444		152
737.5	444	—5.5	1	30.25	1	5.5	
740	480	—3	37	9	1369	111	
744.1	422	1.1	—21	1.21	441	23.1	
745	480	2	37	4	1369		74
744.1	442	1.1	—1	1.21	1	1.1	
739.1	442	—3.9	—1	15.21	1		3.9
732.9	432	—10.1	—11	102.01	121		111.1
746	436	3	—7	9	49	21	
756.2	448	13.2	5	174.24	25		66
744.1	426	1.1	—17	1.21	289	18.7	
753.8	445	10.8	2	116.64	4		21.6
741.1	449	4.1	6	16.81	36		24.6
742.9	462	— .1	19	.01	361	1.9	
729.5	422	—3.5	—19	12.25	361		66.5
743.9	436	.9	—7	.81	49	6.3	
744.3	493	1.3	50	1.69	2500		65
747.8	429	4.8	—14	23.04	196	67.2	
740	495	—3	52	9	2604	156	
755.1	402	12.1	—41	146.41	1681	496.1	
				1315.71	17620	1522.	632.1
						632.1	
						—889.9	

$$\sigma_1 = \sqrt{\frac{1315.71}{24}} = 7.4$$

$$\sigma_2 = \sqrt{\frac{17620}{24}} = 27.1$$

$$\Sigma(xy) = -889.9.$$

$$\text{Coefficient of Correlation} = \frac{\Sigma(xy)}{N\sigma_1\sigma_2} = \frac{889.9}{24 \times 7.4 \times 27.1} = -.16$$

$$\text{Regression} = \frac{-16 \times \sigma_2}{\sigma_1} = -.58$$

Relation of Carbon Dioxide Excretion to Barometric Change.

TABLE XI—B, 7 A. M.

Barometer Millimetres	Carbon Dioxide Milligrams	X	Y	X ²	Y ²	Products (xy)	
						Negative	Positive
739	381	—2.6	—97	6.76	9409		252.2
746	489	4.4	11	19.36	121		48.4
745.1	514	3.5	36	12.25	1296		126
726.2	535	—15.4	57	237.16	3249	877.8	
721	488	—20.6	10	424.36	100	260	
742.1	520	.5	42	.25	1764		21
740	529	—1.6	51	2.56	2601	81.6	
737.1	438	—4.5	—40	20.25	1600		180
741.3	416	— .3	—62	.09	2844		18.6
743.5	537	1.9	59	3.61	3481		112.1
743.5	528	1.9	50	3.61	2500		95
732.5	439	—9.1	—39	82.81	1521		354.9
751.5	410	9.9	—68	98.01	4624	673.2	
751.4	455	9.8	—23	96.04	529	225.4	
753.9	453	12.3	—25	151.29	625	307.5	
737.1	543	—4.5	65	20.25	4225	292.5	
746.5	469	—4.9	— 9	24.01	81	44.1	
747.8	418	6.2	—60	38.44	3600	37.2	
739.3	445	—2.3	—33	5.29	1089		75.9
745.5	402	3.9	—76	15.21	5775	295.4	
743.7	399	2.1	—79	4.41	6241	165.9	
749	509	7.4	31	54.76	961		229.4
739.8	500	—1.8	22	3.24	484	39.6	
				1324.02	59721	3301.2	1513.5
						1513.5	
						1787.7	

$$\sigma_1 = \sqrt{\frac{1324.02}{24}} = 7.4$$

$$\sigma_2 = \sqrt{\frac{59721}{24}} = 49.8$$

$$\Sigma (xy) = -1787.7$$

$$\text{Coefficient of Correlation} = \frac{\Sigma (xy)}{N\sigma_1\sigma_2} = \frac{-1787.7}{24 \times 7.4 \times 49.8} = -.2$$

$$\text{Regression} = \frac{-.2\sigma_2}{\sigma_1} = -.13$$

Relation of Carbon Dioxide Excretion to Barometric Change.

TABLE XII—B, 12 M.

Barometer Millimetres	Carbon Dioxide Milligrams	x	y	x ²	y ²	Products (xy)	
						Negative	Positive
739.1	498	—3.6	17	12.96	289	61.2	
746.2	422	—3.5	—59	12.25	3481	206.5	
742.5	429	.2	—52	.04	2704	10.4	
722.1	434	—20.6	—48	424.36	2304		988.8
726.9	507	—15.8	26	249.64	676	410.8	
742.5	553	— .2	72	.04	5184	14.4	
740.1	495	— 2.6	14	6.76	196	36.4	
736.1	489	— 6.6	8	43.56	64	52.8	
742.9	462	.2	19	.04	361	3.8	
745.1	442	2.4	39	5.76	1521	93.6	
743.5	466	.8	—15	.64	225	12	
739.9	525	— 2.8	44	7.84	1936	123.2	
732.9	560	— 2.8	79	7.84	6241	221.2	
745.8	442	3.1	—39	9.61	1521	120.9	
753.2	506	10.5	25	110.25	625		262.5
749.3	422	6.6	—59	43.56	3481	389.4	
753.6	476	10.9	—5	118.81	25	54.5	
747.5	531	4.8	50	23.04	2500		240
748.1	460	5.4	—21	29.16	441	113.4	
747.9	459	5.2	—22	27.04	484	114.4	
740.1	474	— 2.6	—7	6.76	49		18.2
744.1	455	1.4	—26	1.96	676	36.4	
743.9	442	1.2	—39	1.44	1521	46.8	
749.8	442	7.1	—39	50.41	1521	276.9	
738.8	459	— 3.9	—22	15.21	484		85.8
752.9	528	10.2	47	104.4	2209		479.4
				1313.02	40719	2399	2074.7
						2074.7	
						—324.3	

$$\sigma_1 = \sqrt{\frac{1313}{26}} = 7.1$$

$$\sigma_2 = \sqrt{\frac{40719}{26}} = 39.5$$

$$\Sigma(xy) = -324.3$$

$$\text{Coefficient of Correlation} = \frac{(xy)}{N\sigma_1\sigma_2} = \frac{-324.3}{26 \times 7.1 \times 39.5} = -.04$$

$$\text{Regression} = \frac{-.04\sigma_2}{\sigma_1} = -.09$$

Relation of Carbon Dioxide Excretion to Barometric Change.

TABLE XIII—B, 5 P. M.

Barometer Millimetres	Carbon Dioxide Milligrams	x	y	x ²	y ²	Products [xy] Negative	Positive
731.1	567	-2.9	66	8.41	4356	191.4	
747.1	541	5.1	40	26.01	1600		204
718.2	548	-23.8	47	566.44	2209	1118.6	
738.1	498	-3.9	3	15.21	9		11.7
742.5	546	.5	45	.25	2025		22.5
739	518	-3	17	9	289	51	
737.5	476	-4.5	-25	20.25	625		112.5
740	570	-2	69	4	4761	138	
744.1	508	2.1	7	4.41	49		14.7
745	553	3	52	9	2704		156
744.1	515	2.1	14	4.41	196		29.4
739.1	531	-2.9	30	8.41	900	87	
732.9	466	-9.1	-35	82.81	1225		318.5
746	462	4	-39	16	1521	156	
744.1	526	2.1	25	4.41	625		52.5
753.3	504	11.3	3	127.69	9		33.9
747.1	440	5.1	-61	26.01	3721	311.1	
742.9	469	.9	-32	.81	1024	28.8	
739.5	409	-2.5	-92	6.25	8464		230
743.9	432	1.9	-69	3.61	4761	131.1	
744.3	493	2.3	-8	5.29	64	18.4	
747.8	436	5.8	-65	33.64	4225	377	
740	537	-2	36	4	1296	72	
7.55	486	13.1	-15	171.61	225	196.5	
				1157.93	46883	2876.9	1185.7
						1185.7	
						1691.2	

$$\sigma_1 = \sqrt{\frac{1157.93}{24}} = 6.9$$

$$\sigma_2 = \sqrt{\frac{46883}{24}} = 44.2$$

$$\Sigma(xy) = -1691.2$$

$$\text{Coefficient of Correlation} = \frac{\Sigma(xy)}{N\sigma_1\sigma_2} = \frac{1691.2}{24 \times 6.9 \times 44.2} = -.23$$

$$\text{Regression} = \frac{-.23\sigma_2}{\sigma_1} = -.17$$

Relation of Carbon Dioxide Excretion to Barometric Change.

TABLE XIV—C, 7 A. M.

Barometer Millimetres	Carbon Dioxide Milligrams					Products [xy]	
		x	y	x ²	y ²	Negative	Positive
739	406	—3.8	5	14.44	25	19	
746	419	3.2	18	10.24	324		57.6
745.1	422	2.3	21	5.29	441		48.3
726.2	390	—16.6	—11	275.56	121		182.6
721	397	—21.8	—4	475.24	16		87.2
742.1	382	— .5	—19	.25	361		9.5
740	419	— 2.8	18	7.84	324	50.4	
736	390	— 6.8	—11	46.24	121		74.8
737.1	393	—5 .7	— 8	32.49	64		45.6
741.3	394	—1 .5	— 7	2.25	49		10.5
743.5	410	.7	9	49	81		6.3
742.3	449	— .5	48	.25	2304	24	
732.5	406	—10.3	5	106.09	25	51.5	
751.5	390	8.7	11	75.69	121		95.7
751.4	383	8.6	18	73.96	324		154.5
753.9	363	11.1	38	123.21	1444		421.8
737.1	388	—5 .7	13	32.49	169	74.1	
751.2	398	8.4	— 3	70.56	9	25.2	
746.5	402	3.7	1	13.69	1		3.7
748.2	364	5.4	—37	29.16	1369	199.8	
739.3	403	—3 .5	2	12.25	4	7	
745.5	402	2.7	1	7.29	1		2.7
743.7	406	.9	5	.81	25		4.5
749	396	6.2	— 5	38.44	25	31	
739.8	409	— 3	8	9	64	24	
747.9	422	5.1	21	26.01	441		107.1
758.8	423	16	21	256	441		336
				1745.23	8693	506	1734.2
							506
							1228.2

$$\sigma_1 = \sqrt{\frac{1745.23}{27}} = 8$$

$$\sigma_2 = \sqrt{\frac{8698}{27}} = 17.9$$

$$\Sigma(xy) = 1228.2$$

$$\text{Coefficient of Correlation} = \frac{\Sigma(xy)}{N\sigma_1\sigma_2} = \frac{1228.2}{27 \times 8 \times 17.9} = .316$$

$$\text{Regression} = \frac{.316\sigma_2}{\sigma_1} = .7$$

Relation of Carbon Dioxide Excretion to Barometric Change.

TABLE XV—C, 12 M.

Barometer Millimetres	Carbon Dioxide Milligrams			x^2	y^2	Products [xy]	
		x	y			Negative	Positive
749.1	390	— 4.2	—24	17.64	576		100.8
746.2	409	2.9	— 5	8.41	25	14.5	
742.5	403	— .8	—11	.64	121		8.3
722.1	403	—21.2	—11	449.44	121		233.2
726.9	375	—16.4	—39	268.96	1521		639.6
742.5	387	— .8	—27	.64	729		21.6
740.1	381	— 3.8	—33	10.24	1089		105.6
736.1	362	— 7.2	—52	51.84	2704		374.4
738.9	422	— 4.4	8	19.36	64	35.2	
742.9	377	— .4	—37	.16	1369		14.8
745.1	386	1.8	—28	3.24	784	50.4	
739.9	403	— 3.4	—11	11.56	121		37.4
732.9	386	—10.4	—28	108.16	784		291.2
745.8	380	2.5	—34	6.25	1156	85	
753.3	425	9.9	11	98.01	121		108.9
749.3	402	6	—12	36	144	72	
753.6	427	10.2	13	106.09	169		133.9
747.5	396	4.2	—18	17.64	324	75.6	
748.1	459	4.8	45	23.04	2025		216
747.9	442	4.6	28	21.16	784		128.8
740.1	438	— 3.2	26	10.24	676	83.2	
744.1	474	.8	60	.64	3600	48	
743.9	448	.6	34	.36	1156		20.4
749.8	449	6.5	35	42.25	1225		227.5
738.8	460	— 4.5	46	20.25	2116	207	
752.9	468	9.6	54	92.16	2916		518.4
758.4	422	15.1	8	228.01	64		120.8
				1652.08	26484	622.9	3350.5
							622.9
							2627.6

$$\sigma_1 = \sqrt{\frac{1652.08}{27}} = 7.8 \qquad \qquad \qquad = \sqrt{\frac{26484}{27}} = 31.3$$

$$\Sigma(xy) = 2627.6$$

$$\text{Coefficient of Correlation} = \frac{\Sigma(xy)}{N\sigma_1\sigma_2} = \frac{2627.6}{27 \times 7.8 \times 31.3} = .39$$

$$\text{Regression} = \frac{.39\sigma_2}{\sigma_1} = 1.5$$

Relation of Carbon Dioxide Excretion to Barometric Change.

TABLE XVI—C, 5 P. M.

Barometer Millimetres	Carbon Dioxide Milligrams	x	y	x ²	y ²	Products [xy]	
						Negative	Positive
739.1	447	— 2.9	20	8.41	400	58	
747.1	409	5.1	—18	26.01	324	91.8	
741.1	428	— .9	1	.81	1	.9	
718.2	390	—23.8	—37	566.44	1369		880.6
738.1	419	— 3.9	—8	15.21	64		31.2
742.5	456	.5	29	.25	841		14.5
739	374	— 3	—53	9	2809		159
737.5	438	— 4.5	11	20.25	121	49.5	
740	473	— 2	46	4	2116	92	
744.1	422	2.1	— 5	4.41	25	10.5	
745	448	3	21	9	441		63
744.1	396	2.1	—31	4.41	961	65.1	
739.1	476	— 2.9	49	8.41	2401	142.1	
732.9	411	— 9.1	—16	82.81	256		145.6
746	448	4	21	16	441		84
756.2	473	14.2	46	201.64	2116		653.2
744.1	337	2.1	—90	4.41	8100	180.9	
747.1	437	5.1	10	26.1	100		51
742.9	435	.9	8	.81	64		7.2
739.5	429	— 2.5	2	6.25	4	5	
743.9	419	1.9	—8	3.61	64	15.2	
744.3	434	2.3	7	5.29	49		16.1
747.9	429	5.8	2	33.64	4		11.6
740	429	— 2	2	4	4	4	
755.1	428	13.1	1	171.61	1		13.1
	4			1232.69	23076	805.	2130.1
							805
							1325.1

$$\sigma_1 = \sqrt{\frac{1232.69}{25}} = 7.02 \quad \sigma_2 = \sqrt{\frac{23076}{25}} = 30.38$$

$$\Sigma(xy) = 1325.1$$

$$\text{Coefficient of Correlation} = \frac{\Sigma(xy)}{N\sigma_1\sigma_2} = \frac{1325.1}{25 \times 7.02 \times 30.38} = +.248$$

$$\text{Regression} = \frac{.248\sigma_2}{\sigma_1} = 1.07$$

The results of the whole series of experiments are summed up in Table XVII.

TABLE XVII.

General Summary.

Sub- ject	Hour	x^2	y^2	N	σ_1	σ_2	$S(xy)$	Coefficient of correlation, r	Probable error	Regres- sion
<i>A</i>	7 A.M.	1,754.7	24,951	29	7.8	29.3	868.	+0.12	± 0.13	0.45
<i>A</i>	12 M.	1,642.4	27,078	28	7.65	31.1	1,574.6	+0.236	± 0.126	0.95
<i>A</i>	5 P.M.	1,315.71	17,620	24	7.4	27.1	589.9	-0.12	± 0.126	-0.44
<i>B</i>	7 A.M.	1,324.02	59,721	24	7.4	49.8	1,787.7	-0.2	± 0.129	-0.13
<i>B</i>	12 M.	1,313.02	40,919	26	6.9	44.2	818.3	-0.04	± 0.124	-0.09
<i>B</i>	5 P.M.	1,158.7	46,883	25	6.5	64.0	1,926.1	-0.23	± 0.13	-0.17
<i>C</i>	7 A.M.	1,228.2	8,693	27	8.0	17.9	1,228.2	+0.316	± 0.12	0.7
<i>C</i>	12 M.	1,652.0	26,484	27	7.8	31.2	2,627.6	+0.39	± 0.11	1.5
<i>C</i>	5 P.M.	1,232.6	23,076	25	7.02	30.38	1,325.1	+0.248	± 0.125	1.07

Conclusions :

There were indications in this work of an influence of barometric change on carbon dioxide excretion in the case of one subject, *C*, since there were three positive coefficients of correlation having the value of 0.316, 0.39, and 0.248, for morning, noon and evening experiments (perfect correlation would be indicated by a coefficient of 1); a slight direct influence is also indicated in the case of *A*, whose coefficients were 0.12, 0.236 and -0.12. In the case of *B*, whose values of carbon dioxide excretion throughout the work were quite irregular, (See Table XVIII) there were three *negative* coefficients with values of -0.2, -0.04 and -0.23, respectively.

TABLE XVIII.

Carbon Dioxide Excretion in Milligrams per Minute	A Cases			B Cases			C Cases		
	A. M.	M.	P. M.	A. M.	M.	P. M.	A. M.	M.	P. M.
361—370							2	1	
371—380							1	3	1
381—390			1	1			5	5	1
391—400				1			6	1	1
401—410	4	1	2	2		1	8	5	1
411—420	3			2			2	1	3
421—430	5	2	4		3		3	3	6
431—440	4	5	3	2	1	3		1	4
441—450	2	3	7	1	4		1	3	3
451—460	2	4	1	2	4			1	1
461—470	5	4	2	1	2	3		2	
471—480	1	3	2		2	1		1	3
481—480		3		2	1	1			
491—500	1	1	2		2	2			
501—510	1			2	2	2			
511—520		1		2		2			
521—530				2	2	1			
531—540				2	1	2			
547—550				1	1	3			
551—560		1			1	1			
561—570					1	1			

These results are, perhaps, what might have been expected. The barometric change is evidently a minor influence and its effect is therefore liable to be masked by other influences, such as exercise, amount and character of meals, etc. Moreover, the effect of varying barometric pressure upon the muscular endurance noted by Prof. Lombard in his own case has not been verified in the case of other subjects. The writer is of the opinion that if a series of parallel ergographic and respiration experiments were made on a number of subjects, it would be found, in general, that positive effects of barometric changes on muscular endurance are accompanied by positive coefficients of correlation of barometric change with rate of excretion of carbon dioxide.

VI. THE EXCRETION OF CARBON DIOXIDE DURING UNIFORM MUSCULAR WORK, AND ITS RELATION TO THE SECONDARY RISE OF THE PULSE RATE.

1. Method.

About twenty experiments were made to find the general course of the changes in rate of excretion of carbon dioxide resulting from work. The work was done on the bicycle with stationary frame. This is driven by the subject at a uniform rate which is continuously recorded. The graphic record of carbon dioxide excretion is taken on a slowly revolving drum along with records of respiratory movements, revolutions of the bicycle crank shaft, and time in seconds. On a loop of paper passing around two drums and moving more rapidly, the pulse is recorded along with a time curve, giving seconds.

By means of a Morse key and an electric signal on each drum, the corresponding parts of the two records are indicated.

In beginning an experiment, the subject puts on the mask, mounts the wheel, the pneumograph and pulse tambour are adjusted and tested, and then the mask is connected to the tubes leading to the apparatus for determining carbon dioxide. The drums are started, and the subject sits quietly on the bicycle until sufficient length of record has been made to show the normal rate of pulse, breathing, and excretion of carbon dioxide. Then, at a signal from the experimenter he begins to drive the wheel in unison with a metronome placed before him, and the records continue. The balance is handled as described in the preceding section. The electric signal connected with the bicycle indicates the moment of starting and stopping, and the speed of revolution. On cessation of the work the records continue until the rate of excretion has returned approximately to what it was before the work began, as indicated by the slant of the line described by the recording lever. The experiment then ends. A record taken in this way is shown in Fig. 7.

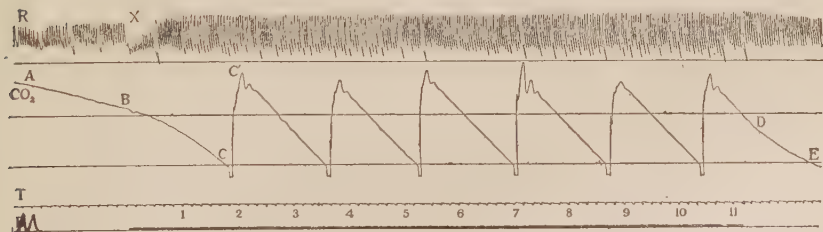


Figure 7 — Graphic record of carbon dioxide excretion during bicycling. To be read from left to right. R, respiratory movements. CO₂ record made by chemograph. The descending lines, as A C, are due to accumulation of carbon dioxide in the absorbing apparatus. The ascending lines, as C 1, form no proper part of the curve but are due to addition of weights by the operator. T is the time marked every 10 seconds. M, revolutions of bicycle crank.

Pulse rate
per minute

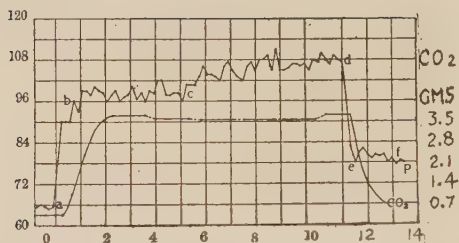


FIGURE 8.— Plotted curves of pulse rate and of carbon dioxide excretion from same experiment as figure 7. Broken line, pulse rate; solid line, carbon dioxide excretion. Ordinates give pulse rate per minute and grams of carbon dioxide per minute.

2. Results.

This figure shows in a general way, the effect of the work on the excretion of carbon dioxide. Beginning at the left, the nearly straight slanting line, A.B., drawn by the writing lever of the chemograph indicates the rate of excretion during rest. Then when work begins, the increased slant of B.C. indicates an increased excretion, and this increase continues for about two minutes. From this time to the end of the working period the slant of the line remains about the same, indicating uniform excretion of carbon dioxide. As soon as work stops there is an immediate change in the slant D.E., showing the diminished excretion.

A more accurate idea of the changes in question can be obtained from Fig. 8, which was obtained from the record of Fig. 7, by careful measurements and plotting. This figure also contains the plotted curve of pulse rate. The pulse curve shows plainly a rapid primary rise, a. b.; a plateau, b. c.; and a slow secondary rise. The curve of carbon dioxide rises rather rapidly during the first two minutes, which includes the period of rapid rise of pulse rate and a part of the plateau. During the remainder of the working period the rate of excretion is seen to be practically constant, 21a although the pulse rate is rising for the latter half of the time. On cessation of work the excretion diminishes, until at the end of two minutes it has returned to practically the original rate. At the same time the pulse rate, although falling rapidly at first (de) is oscillating about a rate (ef) 20 per cent above the normal.

(c) Discussion of Results:

A comparison of the curves of pulse rate and carbon dioxide then, shows that the primary rise of pulse frequency coincides in time approximately with the rise in excretion of carbon dioxide, and the same can be said of the corresponding fall. The short latent period of the pulse shows, as has been stated by Bowen†, that if the increased pro-

†loc. cit.

duction of carbon dioxide is in any way responsible, even in part, for the change in pulse rate when work begins, the influence must be brought to bear through nervous channels, rather than as a direct effect of the gas upon the heart itself or upon the cardiac centers. There seems to be no reason why the prompt increase in heart action may not be due in part at least to sensory impulses arising in the muscles as a result of the waste products suddenly set free there as advocated by Anthanasiu²⁸.

The results, obtained, then, show no evidence of any relation of cause and effect between the production of carbon dioxide, and the secondary rise in pulse rate. In Fig. 8 it is seen that the excretion of carbon dioxide is constant during the entire period of the secondary rise of pulse rate, while the secondary fall of pulse rate during recovery is continued after the rate of excretion of carbon dioxide has returned to the normal. The lack of correspondence in the two curves practically amounts to a demonstration that the secondary changes in pulse rate have nothing to do with the production of carbon dioxide and its elimination from the system.

VII. THE LATENT PERIOD OF CARBON DIOXIDE EXCRETION

Method:

A number of experiments were made to determine how soon after work begins the increase in production of carbon dioxide begins to show itself in the expired air. Fig. 9 shows a group of records taken in the course of these experiments. The procedure is as follows: The subject, sitting quietly on the bicycle, breathes into the apparatus for about 30 seconds, the rate of excretion of carbon dioxide being recorded on the drum, giving the line m. n. in curve A. He then begins driving the bicycle, the time of starting being accurately indicated by marker M. The experiment continues only long enough to show a definite increase in the excretion of carbon dioxide resulting from the work. After fixing the record in shellac, the point n on the curve of carbon dioxide, where the line first changes its direction as the result of the work, is revolved to the base line with a radius equal to the length of the long arm of the writing lever, so as to avoid error due to rotation of the lever on its axis. Now the number of seconds between the beginning of work and the resulting change in excretion of carbon dioxide can be readily obtained from the time record, T.

To find the result desired we must deduct from the time found in the manner just described, the time required for the passage of the exhaled air from the mouth and nostrils, through the mask and connecting tubes to the chemograph, and sufficient additional time to collect in the soda-lime enough carbon dioxide to overcome the inertia of the balance. The time to be deducted is found as follows: While sitting

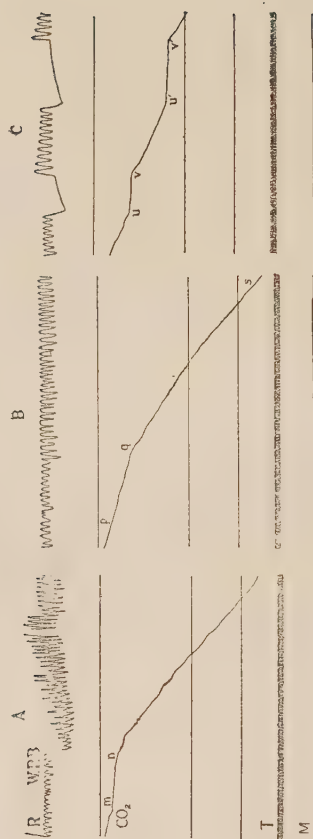


FIGURE 9.—Excretion of carbon dioxide during work and during modified respiratory movements. R, respiratory movements; CO₂, record of chemograph; T, time in seconds; M, bicycle; M, holding the breath. Curve A shows changes due to beginning of work; curve B, deepened respiration followed by work; curve C holding the breath.

quietly upon the bicycle, with the record in progress, the subject holds his breath for several seconds. The result is shown in Curve C of Fig. 9. The pneumograph curve at the top of the record shows when the breath is held. Soon the lever point which records the movement of the balance changes its direction, finally writing the horizontal line U V. When the subject begins to breathe again the pneumograph curve shows the exact moment of the first expiration, and the time from this point to the point V, where the carbon dioxide lever first begins to fall again, is the time of delay due to the apparatus. From a large number of tests this time was found to be close to 6 seconds. Since this delay depends upon the rate at which air is drawn through the apparatus by the suction pump, all of the experiments on latent period were made with the air moving at the uniform rate of 20 litres per minute.

2. Results.

Making the deduction of 6 seconds in the case in curve A of Fig. 9, values for the latent period were obtained varying all the way from 3 to 14 seconds. Now few of these results are long enough to correspond with the time required for the carbon dioxide formed in the muscles at the time of the first muscular contraction to reach the outside air. It must first diffuse into the blood from the tissues where it is formed, then traverse the venous half of the systemic circulation, the right side of the heart, and the arterial half of the pulmonary circulation, and finally diffuse into the air of the alveoli before any of it can appear in the breath. From the latest conclusions of Stewart and others who are considered as authorities on the time of the circulation, it appears that from 15 to 20 seconds is the least possible time for the blood to travel this distance, to say nothing of the diffusion time. We must evidently account for the shortness of the latent period thus found.

Careful study of the matter finally led to the conclusion that the sudden change in rate of excretion of carbon dioxide on beginning work was due primarily to a better ventilation of the lungs while the continuation of the fall was due to the ventilation of the blood and tissues as well.³¹

A recognition of this fact led to the following modification of the methods employed in the determination of the latent period of carbon dioxide excretion.

After the "normal" rate of excretion had been obtained (A B, Fig. 9), the subject began forced breathing at a predetermined rate, continuing this for a minute or so until the curve of carbon dioxide had ap-

parently assumed its permanent direction. At this point, at a signal from the experimenter, the subject began to drive the bicycle as in the preceding experiments.

Curve B of Fig. 9 shows the result in one instance. The effect of the increased respiration is clearly marked, the new rate of excretion or being sharply defined from the normal rate (pq) preceding it. The further increase on beginning work is not so prompt in its appearance and comes on more gradually, reaching its maximum after a minute or more, depending on the work. In these experiments the latent period of increase due to the work was from seventeen to twenty-two seconds. It is evident that as the latent period will vary with the rapidity of the circulation, the rapidity of diffusion, and the rate of work, a more definite figure is not to be expected.

Shortly after the publication of these results by Bowen and the writer, a communication was received from Prof. N. Zuntz, calling attention to the gradual character of the change in rate of excretion of carbon dioxide after the beginning of work (as already mentioned) and kindly suggesting a modification of the method of carrying out the latent-period experiments. According to Prof. Zuntz, if the forced breathing were continued for *five* minutes instead of *one* minute, as already stated, the blood and tissues would become thoroughly ventilated; the direction of the curve of carbon dioxide would become parallel to that before forced breathing began; and furthermore, with the beginning of work, the carbon dioxide curve, after the latent period of twenty seconds, would change much more sharply than it did in the published record. The writer accordingly made a series of experiments in which the forced breathing was continued for from five to seven minutes before bicycle work has begun.

The results of one of these experiments are seen in Figure 10 in which A is the pneumograph record, Pqrs the carbon dioxide curve, T the chronograph record, and M the bicycle record. The line Pq' as in the previous paper,³ represents the rate of excretion before the beginning of forced breathing; the line Pqq'q''r (broken by the arresting of the beam and the addition of four gram weights) represents the curve of carbon dioxide during forced breathing; r is the position on the curve of the carbon-dioxide-writing lever at the instant when work was begun; and s is the point where the curve changes as a result of the work.

This research was conducted on two subjects. It was found very difficult to maintain respiration of uniform depth for five minutes, since there is a decided tendency to make the respiration shallower. Indeed, notwithstanding the great care on the part of the subject, the

³Higley and Bowen: *Loc. cit.*

pneumograph record indicated, in some cases, a lessened depth of respiration toward the end of the forced respiration period.

In the case of one subject the curve for rate of excretion of carbon dioxide returned, during the period of forced respiration, practically to the original value. With the other subject the return was less perfect. It would seem that as a result of the additional work of the respiratory organs a return of the rate of excretion to the value during normal respiration could not be expected.

While, therefore, the writer is able to confirm Prof. Zuntz's prediction regarding the sharpness of the change, as a result of work, in the curve of carbon dioxide after continued forced respiration, he can only confirm in part Prof. Zuntz's prediction on the return of the curve during forced respiration, to the direction which it had before forced respiration was begun.



FIGURE 11.—The Latent Period of Carbon Dioxide Excretion. Curve of CO_2 Excretion, $\text{L} \cdot \text{min}^{-1}$, vs. s. Respiration, A; Time, T. Water, Bicycle/M

CONCLUSIONS

1. The problem of finding the changes in rate of excretion of carbon dioxide resulting from muscular work and other causes is practically solved by the method used in this research.

2. The latent period of increase in excretion of carbon dioxide from the lungs in case of beginning work is approximately twenty seconds, and the increase reaches its maximum in about two minutes.

3. The rate of excretion of carbon dioxide from the lungs is practically uniform from minute to minute during uniform muscular work, after the blood has had time to take part fully in the process of elimination.

4. Upon cessation of work the excretion of carbon dioxide decreases to the normal amount in about the time occupied by its increase, and after a like latent period.

5. The results obtained show no indication of any connection of cause and effect between the production and elimination of carbon dioxide and the secondary rise of pulse rate.

GENERAL SUMMARY

1. In the balance-chemograph we have an apparatus which will be of service in a study of the rate of change of a number of chemical reactions.

2. The respiration apparatus of which the chemograph forms a part can be employed with advantage in a study of the character of all important changes in the rate of excretion of carbon dioxide from the lungs; furthermore, with this apparatus the analyses and calculations that are necessary in experiments on the respiration, are greatly simplified.

3. The average carbon dioxide excretion per kilogram of body weight per minute in the case of 24 normal subjects, at a time averaging four hours after the midday meal was .0063 grams. This agrees well with values obtained by Johannsen and Magnus-Levy.

4. The daily curve of metabolism is affected by the time of taking the heartiest meal. Indigestion, catarrhal infection and thorough athletic training increased the rate of excretion and the presence in the body of the subject of a large amount of adipose tissue diminished the rate of excretion.

5. A series of experiments made daily, morning, noon and evening, for five weeks, seems to show that with some subjects the carbon dioxide excretion varies with the barometric height. This result is in harmony with results obtained by Lombard on the effect of barometric changes on muscular endurance.

6. By the use of the respiration apparatus described in this paper the rate of change of carbon dioxide excretion from a condition of rest through a period of uniform muscular work and the period of recovery has been worked out. This curve is markedly different at important points from the corresponding pulse curve as worked out by Bowen. The secondary rise in the pulse rate is not due to the presence of an increased amount of carbon dioxide in the blood.

7. The latent period of carbon dioxide excretion as a result of vigorous work is about 20 seconds.

8. After a period of forced respiration lasting five minutes, the curve of excretion of carbon dioxide nearly returns to the direction which it had before forced respiration began; if now vigorous muscular work be begun, the curve of excretion of carbon dioxide shows a much more sharp turn than in the case where the period of forced breathing is much more brief.

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